? b 155
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File 155:MEDLINE(R) 1966-2000/Oct W4
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Set Items Description
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S1 38296 HEPATITIS(W)B
S2 149570 POLYMERASE
S3 2424 S1 AND S2
S4 271351 MUTANT? OR MUTAT?
S5 544 S3 AND S4
S6 163 S4(5N)S2 AND S1
S7 9029427 PY<1997
S8 84 S6 AND S7
? t s8/7/1-3

8/7/1
DIALOG(R)File 155:MEDLINE(R)
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09010371 97000173
Generation of duck hepatitis B virus polymerase mutants through site-directed mutagenesis which demonstrate resistance to lamivudine [(--)-beta-L-2', 3'-dideoxy-3'-thiacytidine] in vitro.
Fischer KP; Tyrrell DL
Department of Medical Microbiology and Immunology, University of Alberta, Edmonton, Canada.
Antimicrobial agents and chemotherapy (UNITED STATES) Aug 1996, 40 (8) p1957-60, ISSN 0066-4804 Journal Code: 6HK
Languages: ENGLISH
Document type: JOURNAL ARTICLE
Hepatitis B virus replication is very sensitive to lamivudine. A single amino acid change in human immunodeficiency virus reverse transcriptase is responsible for high-level resistance to this compound. Duck hepatitis B virus mutants were created bearing the analogous amino acid change in the duck hepatitis B virus polymerase. Viral DNA production was reduced 92% for the wild-type virus at 2 micrograms of lamivudine per ml, while the mutants required 40 micrograms of lamivudine per ml to inhibit replication by greater than 80%.

8/7/2
DIALOG(R)File 155:MEDLINE(R)
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09006414 96374966
Mutation in HBV RNA-dependent DNA polymerase confers resistance to lamivudine in vivo.
Tipples GA; Ma MM; Fischer KP; Bain VG; Kneteman NM; Tyrrell DL
Department of Medical Microbiology and Immunology, Glaxo Wellcome-Heritage Research Institute, University of Alberta, Edmonton, Canada.
Hepatology (UNITED STATES) Sep 1996, 24 (3) p714-7, ISSN 0270-9139 Journal Code: GBZ
Languages: ENGLISH
Document type: JOURNAL ARTICLE
The (-) enantiomer of 3'-thiacytidine (lamivudine) has been found to be a potent inhibitor of hepatitis B virus (HBV) and human immunodeficiency virus (HIV) replication. Mutation of methionine to valine or isoleucine at the YMDD (tyrosine, methionine, aspartate, aspartate) motif of the HIV reverse transcriptase has been shown to be responsible for lamivudine resistance in HIV. The hepadnaviruses also have the YMDD motif in their DNA polymerase. Therefore, it is possible that hepadnaviruses could develop lamivudine resistance by a similar mutation at this motif. We analyzed the HBV from a liver transplantation patient who developed recurrent HBV viremia during lamivudine treatment. The polymerase gene was amplified by polymerase chain reaction (PCR), and the region coding for the YMDD motif was sequenced. The pretreatment HBV sequence coded for YMDD, while the lamivudine-resistant mutant HBV coded for YIDD (tyrosine, isoleucine, aspartate, aspartate). With the documented changes in the YMDD motif of lamivudine-resistant HIV, it is likely that the methionine-to-isoleucine mutation in the YMDD motif of the HBV polymerase contributes significantly to the lamivudine-resistance of HBV isolated from this patient.

8/7/3
DIALOG(R)File 155:MEDLINE(R)
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09006413 96374965
Selection of mutations in the hepatitis B virus polymerase during therapy of transplant recipients with lamivudine.
Ling R; Mutimer D; Ahmed M; Boxall EH; Elias E; Dusheiko GM; Harrison TJ
University Department of Medicine, Royal Free Hospital School of Medicine, London, UK.
Hepatology (UNITED STATES) Sep 1996, 24 (3) p711-3, ISSN 0270-9139 Journal Code: GBZ
Languages: ENGLISH
Document type: JOURNAL ARTICLE
We describe mutations in the hepatitis B virus (HBV) polymerase gene in viruses which reactivated in two patients during therapy with -2'-deoxy-3'-thiacytidine, or lamivudine (3TC), and following orthotopic liver transplantation for chronic hepatitis B. Virus resistance to 3TC is

associated with mutations which lead to amino acid substitutions in the highly conserved tyr-met-asp-asp (YMDD) motif, part of the active site of the polymerase, and which parallel those seen in resistant human immunodeficiency virus (HIV). Substitutions of valine and isoleucine for methionine were found in the two cases. The significance of single secondary mutations, which differ between viruses from the two patients, remains to be determined. Thus, viral resistance to lamivudine of hepatitis B virus mimics that of HIV and can occur in the setting of immunosuppression after liver transplantations.

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